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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/932,128	08/16/2001	Juan Yguerabide	A9372	5342

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EXAMINER	
YANG, NELSON C	
ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/932,128	YGUERABIDE ET AL.	
	Examiner	Art Unit	
	Nelson Yang	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *49-52,55,71-73,76,80,84,166-172,176-181 and 217-220* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *49-52, 55, 71-73, 76, 80, 84, 166-172, 176-181, 217-220* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicant's amendment of claims 49, 76, 84, is acknowledged and has been entered.

2. Applicant's addition of claims 219, 220, is acknowledged and has been entered.

3. Claims 49-52, 55, 71-73, 76, 80, 84, 166-172, 176-181, 217-220 are currently pending and under examination.

Rejections Withdrawn

4. Applicant's arguments, see amended claims, filed July 17, 2009, with respect to the rejections of 49-52, 55, 76, 166-172, 176-179, 217, 218 under 35 U.S.C. 103(a) as being unpatentable over Nicoli et al. [US 4,647,544] in view of Roth [Roth, The preparation of protein A-gold complexes with 3nm and 15 nm gold aprticles and their use in labeling multiple antigens on ultra-thin sections, 1982 Histochemical Journal 14: pp.791-801] have been fully considered and are persuasive. In particular, the Office notes that Roth explicitly excludes gold particles larger than 20 nm in diameter. The rejection of claims 49-52, 55, 76, 166-172, 176-179, 217, 218 under 35 U.S.C. 103(a) has therefore been withdrawn.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 49-52, 55, 166, 168, 172, 218 are rejected under 35 U.S.C. 102(b) as being anticipated by Bendayan [Bendayan, Double immunocytochemical labeling applying the protein A-gold technique, 1982, J Histochem Cytochem, 30(1):pp.81-85].

With respect to claims 49, 218, Bendayan however, teach making monodispersed colloidal gold suspensions with particles of 125 ± 2 Å in diameter which would be less than 5% variation, and further teach these particle suspensions are coupled with protein A allow for detection of antigenic sites that are present only at the surface of tissue sections, and that the specificity of particle diameters allow for multiple complexes with different diameters to be used for double labeling (p.82, col.2, p. 83, col.2). Although Bendayan do not specify that the gold particles are further coated with a surface coat of gold, the surface of the colloidal gold particles taught by Bendayan would also be gold, and therefore the particles would structurally be the same. Furthermore, the gold particles of Bendayan would inherently have a maximum absorption wavelength between 575 nm and 635 nm.

7. With respect to claims 50-52, 166, 168, 172, Bendayan teaches particle suspensions comprising particles of 125 ± 2 Å in diameter that are coupled with protein A (p.82, col.2).

8. With respect to claim 55, Bendayan et al. teach spherical proteins (p.82, fig. 1).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 49-52, 55, 76, 166-172, 176-179, 217, 218 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nicoli et al. [US 4,647,544] in view of Bendayan [Bendayan, Double immunocytochemical labeling applying the protein A-gold technique, 1982, J Histochem Cytochem, 30(1):pp.81-85].

With respect to claims 49, 166, Nicoli et al. teach colloidal gold particles which have been coated with a variety of macromolecules such as avidin, lectins, IgG in the size range 5 to 100 nm (column 15, lines 15-25), which would therefore have the inherent feature of maxiumum wavelength absorption from 525 nm to about 635 nm, as evidenced by applicant's own specification (see para. 254, table 2). Although Nicoli et al. do not specify that the gold particles are further coated with a surface coat of gold, the surface of the colloidal gold particles taught by Nicoli et al. would also be gold, and therefore the particles would structurally be the same. These particles are found in homogenous immunoassays where analytes are detected using optical interference and specifially a Bragg scattering peak (column 5, lines 58-65). Nicolo et al. fail to teach that the coefficient of variation in size of the population of particles is less than 5%.

Bendayan et al., however, teach making monodispersed colloidal gold suspensions with particles of 125 ± 2 Å in diameter which would be less than 5% variation, and further teach these particle suspensions allow for detection of antigenic sites that are present only at the surface of tissue sections, and that the specificity of particle diameters allow for multiple complexes with different diameters to be used for double labeling (p.82, col.2, p. 83, col.3).

Furthermore although neither Nicoli et al. or Bendayan et al. do not specify that the particles have a maxium absorption wavelengths of from about 525 nm to about 635 nm, this would be an inherent feature of the gold particles taught by Nicoli et al. and Bendayan, as the

particles have diameters that fall within the ranges disclosed by applicant that would result in a maxium absorption wavelengths of from about 525 nm to about 635 nm.

Therefore, it would have been obvious for the microspheres of Nicoli et al. to have precise size ranges varying no more than 5%, as this would allow for the visualization of two different antigens when used in conjunction with a second population of monodisperse particles of a different size. It would further have been obvious for the particles have to a maxium absorption wavelengths of from about 525 nm to about 635 nm through normal optimization procedures known in the art.

11. With respect to claims 50-52, Nicoli et al. teach colloidal gold particles coated with avidin and IgG (column 15, lines 25-35). Although Nicoli et al. do not specifically recite that proteins do not significantly interact with light in the visible region of the spectrum, this property is inherent in proteins, and therefore would be taught by the invention ofNicoli et al. and Bendayan.

12. With respect o claim 55, the particles taught by Nicoli et al. are spherical (fig. 4C).

13. With respect to claim 76, Nicoli et al. teach colloidal gold particles which have been coated with a variety of macromolecules such as avidin, lectins, IgG in the size range of 20 to 500 nm (column 15, lines 25-35)

14. With respect to claim 167, Nicoli et al. teach different specific antibodies for binding to different antigens (column 23, lines 42-55).

15. With respect to claims 168-172, 176-179, 217, 218, Nicoli et al. teach colloidal gold particles which have been coated with a variety of macromolecules such as avidin, lectins, IgG in the size range of 20 to 500 nm (column 15, lines 25-35),

16. With respect to claims 219, 220, Nicoli et al. teach colloidal gold particles in the size range 5 to 100 nm which have been coated with a variety of macromolecules such as avidin, lectins, IgG (column 15, lines 15-25). Although neither Nicoli et al. or Bendayan et al. do not specify that the particles have a maxium absorption wavelengths of from about 525 nm to about 635 nm, this would be an inherent feature of the gold particles taught by Nicoli et al. and Bendayan, as the particles have diameters that fall within the ranges disclosed by applicant that would result in a maxium absorption wavelengths of from about 525 nm to about 635 nm. Furthermore, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranged involves only routine skill in the art. *In re Aller*, 105 USPQ 233. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to obtain particles with a diameter of about 60 nm to 100 nm or 80 nm, with a maximum absorption wavelength of about 545 nm to 575 nm, or 555 nm, through normal optimization procedures known in the art.

17. Claims 71-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nicoli et al. [US 4,647,544] in view of Bendayan [Bendayan, Double immunocytochemical labeling applying the protein A-gold technique, 1982, J Histochem Cytochem, 30(1):pp.81-85], as applied to claim 49 above, and further in view of Rembaum et al. [US 4,929,400].

With respect to claims 71-72, Nicoli et al. and Bendayan teach the invention as discussed above, but fail to explicitly teach that the gold particles comprise a magnetic or ferroelectric material.

Rembaum et al., however, teach microspheres created from polymers, proteins, waxes, starches, glasses, magnetic, and metals to impart various different properties to the particles (column 3, lines 40-50, column 4, lines 35-50), and having precise size range with diameters below 1000 Angstroms (column 8, lines 41-54, lines 55-69). Rembaum et al. further teach that the microspheres may comprise magnetic material (column 4, lines 1-10), in order to allow for magnetic separation of analytes from a mixture (column 7, lines 35-60).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention for the particles of Nicoli et al. to comprise magnetic material, so that analytes may be separated from a mixture magnetically, and to impart various different optical properties to the particles.

18. Claims 71-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bendayan [Bendayan, Double immunocytochemical labeling applying the protein A-gold technique, 1982, J Histochem Cytochem, 30(1):pp.81-85] in view of Rembaum et al. [US 4,929,400].

19. With respect to claims 71-72, Bendayan teach the invention as discussed above, but fail to explicitly teach that the gold particles comprise a magnetic or ferroelectric material.

Rembaum et al., however, teach microspheres created from polymers, proteins, waxes, starches, glasses, magnetic, and metals to impart various different properties to the particles (column 3, lines 40-50, column 4, lines 35-50), and having precise size range with diameters below 1000 Angstroms (column 8, lines 41-54, lines 55-69). Rembaum et al. further teach that the microspheres may comprise magnetic material (column 4, lines 1-10), in order to allow for magnetic separation of analytes from a mixture (column 7, lines 35-60).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention for the particles of Bendayan to comprise magnetic material, so that analytes may be separated from a mixture magnetically, and to impart various different optical properties to the particles.

20. Claims 73, 80, 84, are rejected under 35 U.S.C. 103(a) as being unpatentable over Nicoli et al. [US 4,647,544] in view of Bendayan [Bendayan, Double immunocytochemical labeling applying the protein A-gold technique, 1982, J Histochem Cytochem, 30(1):pp.81-85], as applied to claim 49 above, and further in view of Rembaum et al. [US 4,929,400], and Siiman et al. [US 5,552,086].

With respect to claims 73, 80, 84, Nicoli et al. and Bendayan teach the invention as discussed above, but fail to explicitly teach that the gold particles comprise a magnetic or ferroelectric material or silver.

Rembaum et al., however, teach microspheres created from polymers, proteins, waxes, starches, glasses, magnetic, and metals to impart various different properties to the particles (column 3, lines 40-50, column 4, lines 35-50), and having precise size range with diameters below 1000 Angstroms (column 8, lines 41-54, lines 55-69). Rembaum et al. further teach that the microspheres may comprise magnetic material (column 4, lines 1-10), in order to allow for magnetic separation of analytes from a mixture (column 7, lines 35-60).

Siiman et al. further disclose that using microstructural gold or silver bumps on microspheres, gold and silver coated particles can be distinguished from each other (column 3,

lines 28-50), as they would be with finely dispersed pure gold or silver particles of the same size (column 4, lines 5-15).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention for the particles of Nicoli et al. to comprise magnetic material and silver, as suggested by Rembaum et al. and Siiman et al., so that analytes may be separated from a mixture magnetically, and to impart various different optical properties to the particles such that different populations of particles would be distinguishable from one another, thus allowing for labeling of different analytes and antigens.

21. Claims 73, 80, 84, are rejected under 35 U.S.C. 103(a) as being unpatentable over Bendayan [Bendayan, Double immunocytochemical labeling applying the protein A-gold technique, 1982, J Histochem Cytochem, 30(1):pp.81-85] in view of Rembaum et al. [US 4,929,400], and n view of Siiman et al. [US 5,552,086].

With respect to claims 73, 80, 84, Bendayan teach the invention as discussed above, but fail to explicitly teach that the gold particles comprise a magnetic or ferroelectric material or silver.

Rembaum et al., however, teach microspheres created from polymers, proteins, waxes, starches, glasses, magnetic, and metals to impart various different properties to the particles (column 3, lines 40-50, column 4, lines 35-50), and having precise size range with diameters below 1000 Angstroms (column 8, lines 41-54, lines 55-69). Rembaum et al. further teach that the microspheres may comprise magnetic material (column 4, lines 1-10), in order to allow for magnetic separation of analytes from a mixture (column 7, lines 35-60).

Siiman et al. further disclose that using microstructural gold or silver bumps on microspheres, gold and silver coated particles can be distinguished from each other (column 3, lines 28-50), as they would be with finely dispersed pure gold or silver particles of the same size (column 4, lines 5-15).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention for the particles of Bendayan to comprise magnetic material and silver, as suggested by Rembaum et al. and Siiman et al., so that analytes may be separated from a mixture magnetically, and to impart various different optical properties to the particles such that different populations of particles would be distinguishable from one another, thus allowing for labeling of different analytes and antigens.

22. Claims 180, 181 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nicoli et al. [US 4,647,544] in view of Bendayan [Bendayan, Double immunocytochemical labeling applying the protein A-gold technique, 1982, J Histochem Cytochem, 30(1):pp.81-85], as applied to claim 49 above, and further in view of Tarcha et al. [US 5,567,628].

With respect to claims 180, 181, Nicoli et al. discloses populations of gold particles and further comprising antibodies, but fails to teach that the antibodies are anti-biotin, anti-fluorescein or anti-digoxinin antibodies.

Tarcha et al., however teach the use of anti-biotin antibodies as a means for attaching biotinylated antibodies (column 23, lines 20-45), thus rendering the particles much more versatile.

Therefore it would have been obvious in the invention of Nicoli et al. and Bendayan et al. to have particles comprising anti-biotin antibodies, as suggested by Tarcha et al., due to the greater versatility it provides the particles, allowing a greater variety of different antibodies to be attached.

23. Claims 180, 181 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bendayan [Bendayan, Double immunocytochemical labeling applying the protein A-gold technique, 1982, J Histochem Cytochem, 30(1):pp.81-85] in view of Tarcha et al. [US 5,567,628].

With respect to claims 180, 181, Bendayan discloses populations of gold particles and further comprising proteins interacting with antibodies, but fails to teach that the antibodies are anti-biotin, anti-fluorescein or anti-digoxinin antibodies.

Tarcha et al., however teach the use of anti-biotin antibodies as a means for attaching biotinylated antibodies (column 23, lines 20-45), thus rendering the particles much more versatile.

Therefore it would have been obvious in the invention of Bendayan et al. to have particles comprising anti-biotin antibodies, as suggested by Tarcha et al., due to the greater versatility it provides the particles, allowing a greater variety of different antibodies to be attached.

Response to Arguments

24. Applicant's arguments with respect to claims 49-52, 55, 71-73, 76, 80, 84, 166-172, 176-181, 217-220 have been considered but are moot in view of the new ground(s) of rejection.

25. The Office, however, would like to note that based on applicant's arguments and on the specification, it would appear that applicant's believe that the novelty of applicant's invention lies in how the particles are made (i.e., the method of making the particles), not necessarily in the particles themselves (i.e., the product). In particular, the prior art clearly discloses the desirability of having monodisperse particles, which is to say, particles of a specific size and shape. Therefore, one of ordinary skill in the art at the time of the invention would have found it obvious that upon reading the phrase "monodisperse particles", that they would have found it obvious to obtain particles that were the same size, with as little variation as possible, to specifically avoid the disadvantages that come from having polydisperse particles. From the specification, it would appear, however, that what applicants have discovered is a method for particle growing which gives narrower size distributions than those available commercially that avoids manually selecting or filtering particles to obtain monodisperse particles (see p.85-86). However, the method of making does not have sufficient patentable weight to render the claims, which are drawn to the product, non-obvious. Furthermore, other methods of obtaining monodisperse particles would still read on the product claims, as discussed above.

26. For these reasons, applicant's arguments are not found persuasive.

Conclusion

27. No claims are allowed.

28. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

29. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571)272-0826. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on (571)272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

30. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nelson Yang/
Primary Examiner, Art Unit 1641